95. (new) The composition of claim 1 in oral dosage form.

~~96~~. (new) A composition comprising at least one antisense oligonucleotide in an emulsion and at least one bile salt.

REMARKS

I. Claim status

Upon entry of the above amendments, claims 1, 4-7, 10, 12, 13, 15, 17, 19, 20, 80, 84, and 85 will be pending in this application. Claims 2, 3, 46, 48-63, 83, and 86 have been canceled without prejudice to their presentation in a continuing application. Claims 87-96 have been added. Support for the added claims can be found throughout the specification and in the original claims. Claim 1 has been amended. Support for the amendment can be found throughout the specification and, for example, in original claims 2 and 3. No new matter has been added.

Applicant also would like to respectfully note a discrepancy with respect to the status of claims 18 and 64. The Office Action Summary lists claims 18 and 64 as pending, however, the present Office Action states that Applicant's submission of November 20, 2001, which requests cancellation of claims 18 and 64, has been entered. Thus, claims 18 and 64 are no longer pending.

II. The claims are novel

The Kawai reference

Claims 1-3, 5-7, 10, 17, 19-20, 46, 48, 54, 59-60, and 62-63 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by unexamined Japanese Patent Application No. 7-330614 (hereinafter "Kawai"). Applicant respectfully traverses the rejection because Kawai fails to teach or suggest all the elements of the present invention.

To anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.*, 334

U.S.P.Q.2d 1565 (Fed. Cir. 1995). Kawai fails to disclose every feature of the claimed invention because Kawai fails to teach or suggest, *inter alia*, a dosage form suitable for non-parenteral administration.

Because Kawai fails to teach or suggest every element of the invention, the claims are not anticipated. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(b).

The Hnatowich Reference

Claims 1-2, 4-7, 15, 46, 52-53, 55-58, and 84 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Pat. No. 5,980,861 (hereinafter "Hnatowich"). Applicant respectfully traverses the rejection because Hnatowich fails to teach or suggest every element of the claimed invention. For example, Hnatowich fails to teach or suggest modulation of expression of a cellular adhesion protein, modulation of a rate of cellular proliferation, or biological activity against eukaryotic pathogens or retroviruses. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(e).

The New Reference

Claims 46, 52-53, 56-57, and 59-61 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Pat. No. 5,853,748 (hereinafter "New"). Applicant respectfully traverses the rejection, however, due to the cancellation of claim 46, the rejection is rendered moot. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(e).

The Bennett Reference

Claims 46, 48-54 and 83 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Pat. No. 5,843,738 (hereinafter "Bennett"). Applicant respectfully traverses the rejection, however, due to the cancellation of claim 46, the rejection is rendered moot. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(e).

The Nielson Reference

Claims 46, 48, 53-54, 59-60, 63 and 86 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by WO 97/13528 (hereinafter "Nielson"). Applicant traverses the rejection and respectfully points out that Nielson cannot qualify as a reference under section 102(e) because no PCT publication with an international filing date prior to November 29, 2000 has a 102(e) date. Nevertheless, due to the cancellation of claim 46, the rejection is rendered moot. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(e).

III. The claims are not obvious

Claims 12-13, 60-61, 80, and 85 stand rejected under 35 U.S.C. § 103 as allegedly being obvious over Kawai in view of New, Bennett and Nielson. Applicant respectfully traverses the rejection because the Office Action has failed to make a *prima facie* case of obviousness.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992). When assessing whether or not a combination of references would have produced a claimed invention, one must consider the teaching of each reference **as a whole** without undue emphasis on those features that would support a finding of obviousness. *In re Wesslau*, 147 U.S.P.Q. 391 (C.C.P.A. 1965)(it is impermissible to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what the references fairly suggest to one of ordinary skill in the art).

The Office Action incorrectly asserts that motivation for combining the bile salts of New with the compositions of Kawai arises because bile salts can improve absorption of biologically active materials into cells. This alleged motivation is insufficient because

the Office Action fails to consider each of the cited references as a whole. For example, the Office Action appears not to have appreciated fully that the intent of New was to counter the low therapeutic index of bile salts by employing a buffer to change the pH of the gut in the oral delivery of a drug. One having skill in the art would understand from New that bile salts without a suitable buffer can be toxic, have a low therapeutic index, and are thus undesirable as penetration enhancers (see, e.g., col. 2, lines 31-54). Thus, there would be no motivation to include a bile salt as a penetration enhancer in the compositions of Kawai. Further, one skilled in the art would understand from New that the bile salt/buffer combinations (devised to overcome the aforementioned toxicity) are intended for solid, oral dosage form, and are therefore poorly suited for liquid formulations such as the emulsion compositions of Kawai (see, e.g., col. 7, lines 36-55). Accordingly, one skilled in the art, *reading the references as a whole*, would not find motivation to combine a bile salt with the compositions of Kawai. ("[F]ocusing on the obviousness of substitutions and differences, instead of the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." *Gillette Co. v. S.C. Johnson & Son*, 16 U.S.P.Q.2d 1923, 1927 (Fed. Cir. 1990)).

The Office Action also fails to provide legally sufficient motivation for combining the antiviral ISIS-2922 in Nielson with the compositions of Kawai. In the Office Action, motivation is improperly said to arise because the compositions of Kawai are intended to provide carriers for "transducing gene DNA" associated with viral illness. However, the cited art provides no reason or suggestion why one skilled in the art would select ISIS-2922 over the numerous other antivirals listed in Nielson (see, e.g., page 3, lines 17-30). Indeed, the Office Action appears to improperly pick and choose from the disclosure of Nielson without any basis to do so and without considering the reference as a whole, as discussed above.

The Office Action further fails to provide legally sufficient motivation for combining any oligonucleotide of Bennett with the compositions of Kawai. Motivation is improperly said to arise because the compositions of Kawai are intended to provide carriers for "transducing gene DNA" that inhibits the expression of genes associated with cancer. However, the cited art provides no reason or suggestion any reason why one

skilled in the art would select an oligonucleotide having a sequence according to SEQ ID NO: 1 from the 84 other antisense oligonucleotides reported in Bennett that can also be useful for treating cancer. Again, it appears the Office Action has improperly picked and chosen from among the cited references without any legally sufficient basis to do so.

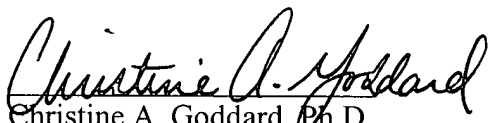
Because the Office Action has failed to point to sufficient motivation for combining the cited references, *prima facie* obviousness has not been met. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 103.

IV. Conclusion

In view of the foregoing, Applicant submits that the claims as amended are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 2, 3, 46, 48-63, 83, and 86 have been cancelled.

Please amend claim 1 according to the marked up version below.

1. (amended) A composition in dosage form suitable for non-parenteral administration comprising at least one antisense oligonucleotide in an emulsion and at least one penetration enhancer selected from the group consisting of surfactants, fatty acids, bile salts, chelating agents, non-chelating non-surfactant molecules, and combinations thereof, wherein said antisense oligonucleotide modulates expression of a cellular adhesion protein, modulates a rate of cellular proliferation, or has biological activity against eukaryotic pathogens or retroviruses.